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EXAMINER
SPIEGLER, ALEXANDER H

ART UNIT	PAPER NUMBER
1637	17

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Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)	
09/673,779	JANSEN ET AL.	
Examiner	**Art Unit**	
Alexander H. Spiegler	1637	

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 January 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

Attachments:

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 7
4) ☐ Interview Summary (PTO-413) Paper No(s).
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other

DETAILED ACTION

1. This action is in response to Paper No. 18, filed on January 31st, 2003. Currently, claims 1-23 are pending. This action is made NON-FINAL. Any objections and rejections not reiterated below are hereby withdrawn.

Information Disclosure Statement

2. It is noted, French Patent 2659981 has been considered and a copy of a signed PTO Form 1449 is enclosed herein.

Specification

3. Claim 15 is objected to because SEQ ID NO: 10 should actually recite "SEQ ID NO: 6". This appears to be a typographical error.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 5-7, 13-15, 17, 19 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 5, 13 and 17 over "capable of hybridizing with nucleic acid found in" because it is not clear as to what conditions are necessary for probes to be "capable of hybridizing with nucleic acid found in...". How does one determine whether a probe is "capable of hybridizing with nucleic acid found in...". Furthermore, the claim could be amended to include the language

B) Claims 7, 15 and 19 are indefinite due to the improper expression of alternative limitations. The claims recite, "having", which implies that the group can have members other than A, B, and C without defining what the other members may be. Therefore, the claim is not clear as to the definition of the probe is. "Alternative expressions are permitted if they present no uncertainly or ambiguity with respect to the question of scope or clarity of the claims." One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being 'selected from the group consisting of A, B, and C'." (See MPEP 2173.05(d)).

C) Claims 6 and 14 over "said nucleic acid" because this recitation lacks antecedent basis.

D) Claim 23 over "its properties of reactivity" because it is not clear as to what constitutes a probe's "properties of reactivity". Furthermore, it is not clear as to how one "considers", "the susceptibility to antibiotic treatment". That is, the step of "including a consideration of the susceptibility" appears to be a mental step, and therefore, it is not clear as to how one accomplishes this goal.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 5, 7, 13, 15, 17, 19 and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

35 U.S.C.§ 112, requires, *inter alia*, that a patent specification contain a written description of the invention and the manner and process of making and using it "...in such full clear and concise terms as to enable one skilled in the art... to make and use" the invention. While it is well settled that a patent application need not teach each possible embodiment of the claimed invention, it is manifestly true that written description cannot be settled by reliance on that which has not been achieved in the art, or that which is not disclosed in the specification. That is, a specification is not considered to satisfy the requirement for an adequate written description if it fails to disclose the specific starting materials or conditions for making the invention. (*Genentech, Inc. v. Novo Nordisk*, 108 F3d. 1361, 42 USPQ2d 100. Fed. Cir. 1997), or evidence that the applicants at the time the application was filed, has possession of the claimed invention.

Additionally, *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention. The invention is, for purposes of the written description inquiry, *whatever is now claimed* (See page 1117)." The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed (See *Vas-Cath* at page 1116)."

Applicant's attention is also drawn to the "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1st Paragraph, Written Description Requirement" (published in Federal Register Vol. 66, No. 4 Friday, January 5, 2001 Notices; p. 1099-1111).

> structural chemical formulas, which permit a person skilled in the art to clearly recognize, that applicant had possession of the claimed invention. *An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention…*
>
> Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient..for inventions in emerging and unpredictable technologies, or for inventions characterized by factors not reasonably predictable which are known to one of ordinary skill in the art, more evidence is required to show possession.

(pgs. 1105-1106).

In the instant case, claims 5, 13 and 17 are drawn to "probes capable of hybridizing with nucleic acid found" in a variety of different and distinct bacteria. The specification does not set forth any description of sufficient, relevant, identifying characteristics of these claimed probes so that a person skilled in the art would recognize that the inventor had possession of the claimed invention. It is noted that these claims could comprise thousands of possible probes, since the claims only require that probes are capable of hybridizing with "nucleic acid found in" a variety of different and distinct bacteria, and does not set forth any limiting distinguishing features of the "nucleic acid found in" the bacteria.

Claims 7, 15, and 19 are all drawn to probes comprising "no more than five mismatches with a probe selected from a group consisting of probes **having** a sequence". These claims encompasses thousands of possible probes, wherein the specification does not set forth any

person skilled in the art would recognize that the inventor had possession of the claimed

invention. First, the claims recite, "having", which suggests that the probes could comprise larger sequences than the probes (i.e. SEQ ID NOS) recited in the claims. The specification does not teach any probes that are larger than the recited probes (i.e. SEQ ID NOS), or any sufficient, relevant, identifying characteristics of larger probes. Furthermore, claims 7, 15, 19 and 21 recite, "no more than five mismatches", which suggests that there could be one to five mismatches in any of recited probes (i.e. SEQ ID NOS). This possibility comprises thousands of possible probes. The specification does not set forth any description of sufficient, relevant, identifying characteristics of these claimed probes so that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Applicant has only taught 12 specific probes of the claimed invention (see pg. 13 of the specification).

Accordingly, there is not an adequate written description for the claimed invention.

8. Claims 5, 7, 13, 15, 17, 19 and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NOS: 1-12, does not reasonably provide enablement for "probes capable of hybridizing with nucleic acid found" in a variety of different and distinct bacteria or probes comprising "no more than five mismatches". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Case law has established that "(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. In *In re Fisher*, 427 F.2d 833, 839,

reasonable correlation of the scope of enablement provided by the specification to the

ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. Furthermore, the court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement".

Also, MPEP 2164.01 states:

"Even though the statute does not use the term 'undue experimentation,' it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)."

The *Wands* court outlined several factors to be considered in determining whether a disclosure would require undue experimentation:

> "They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

Id. at 1404.

In the instant case, the specification does not enable one of skill in the art to make and use the claimed invention for the following reasons:

(1) The quantity of experimentation necessary

In order to practice the invention, the practitioner must experiment by creating one to five mismatches in SEQ ID NOS: 1-12, wherein the probes comprising said mismatches can be used

mutated probes could be used in the claimed methods is highly unpredictable, and can only be tested be carrying out the complete claimed method. In essence, the experimentation that one skilled in the art would be required to perform is in fact the proposed novelty of the invention. "(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement". (*Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001).

Therefore, the quantity of experimentation is not only difficult, but also unpredictable.

(2) The amount of direction or guidance presented

The specification teaches that the probes of SEQ ID NOS: 1-12 are capable of carrying out the claimed methods (see pgs. 13, 17 and 19-20).

(3) The presence or absence of working examples

The only working examples use the probes of SEQ ID NOS: 1-12 (see pgs. 16-21).

(4) The nature of the invention

The nature of the invention pertains to the detection of bacteria in samples using nucleic acid probes.

(5) The state of the prior art

The prior art of Leong et al. (EP 0479117, cited in the IDS) teaches that specific nucleic acid probes can be used for bacteria detection using in *situ* hybridization protocols (see pgs. 7-10).

(6) The relative skill of those in the art

probes comprising said mismatches can be used in an "*in situ* hybridization protocol selected on the basis of the outcome of [a] Gram-staining".

(7) The predictability or unpredictability of the art

The unpredictability of finding mismatches in SEQ ID NOS: 1-12, which can be used in the claimed invention, is high, since the specification or state of the art teaches any specific criteria in selecting mutations in SEQ ID NOS: 1-12 that can be used in the claimed method.

(8) The breadth of the claims

The invention is directed to a method for identifying the presence of a bacterium in a sample comprising testing said sample by Gram-staining and testing said sample with a probe according to an *in situ* hybridization protocol selected on the basis of the outcome of said Gram-staining and identifying the presence of the bacterium in the sample.

Accordingly, in view of the unpredictability in the art and in view of the lack of specific disclosure in the specification, undue experimentation would be required to practice the invention as it is claimed.

Applicants are reminded that the enablement requirement of 35 U.S.C. 112, first paragraph, is separate and distinct from the description requirement. Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116-17 (Fed. Cir. 1991).

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1, 2, 4, 6, 20 and 23 are rejected under 35 U.S.C. 102(e) as being anticipated by Hyldig-Nielsen et al. (USPN 5,888,733).

Nielsen teaches a method for identifying the presence of a gram negative, rod bacterium (*Neisseria gonorrhea*) in a sample comprising testing said sample by Gram-staining and testing said sample with a probe according to an *in situ* hybridization protocol selected on the basis of the outcome of said Gram-staining and identifying the presence of the bacterium in the sample (col. 29, Example 29). The reference teaches the sample is a clinical sample; the nucleic acid is ribosomal RNA (col. 29, Example 29).

11. Claims 1-6, 8-18, 20 and 22-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Leong et al. (EP 0479117, cited in the IDS).

Leong teaches a method for testing a sample with a probe according to an *in situ* hybridization protocol selected on the basis of the outcome of a Gram-staining and identifying the presence of the bacterium in the sample (abstract, pgs. 3-6 and Examples 1-8). Leong teaches clinical samples, the determination of the rod or coccus character, rRNA is the template nucleic acid, treatment of the sample with lysozyme, probes capable with hybridizing to many different bacteria, including, E. *aerogenes*, E. *faecalis*, S. *aureus*, positive and negative control probes, a one-step procedure of binding and fixing bacteria simultaneously, as well as genera and

inherent that a Gram stain test must have been carried out prior to the *in situ* hybridization protocol because the hybridization probes chosen were selected on the basis on whether the bacteria was Gram negative or positive. Leong teaches the gram stain test is important in determining the identity of bacteria (pg. 2, ln. 8-20); Leong also teaches that amplification (e.g., PCR) was carried on gram negative and gram-positive bacterial samples before *in situ* hybridization (pgs. 7-9). To have carried out PCR on gram positive and negative bacteria suggests that a gram stain must have been carried out prior to the amplification to ensure that the sample was in fact gram positive or negative. Therefore, while Leong does not specifically teach the testing of a sample by gram staining, it is inherent that a gram stain must have been carried out prior to the *in situ* hybridization protocol, wherein said *in situ* hybridization protocol was based on said gram stain.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 3, 5, 8-18 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hyldig-Nielsen et al. (USPN 5,888,733) as applied to claims 1, 2, 4, 6, 20 and 23 above, and further in view of Leong et al. (EP 0479117, cited in the IDS).

Nielsen teaches a method for identifying the presence of a gram negative, rod bacterium

with a probe according to an *in situ* hybridization protocol selected on the basis of the outcome of said Gram-staining and identifying the presence of the bacterium in the sample (col. 29, Example 29).

Nielsen does not teach methods for identifying gram-positive bacteria or specific types of gram-negative bacteria.

However, identifying both gram-positive and specific types of gram-negative bacteria are well known in the art. For example, Leong teaches the identification of both gram-positive and gram-negative bacteria in order to identify and/or treat septicemia (pg. 2).

Therefore, in view of the teachings of Leong, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the Nielsen's method of performing a gram-staining test on a sample, and then testing said sample with a probe according to an *in situ* hybridization test, selected on the basis on said gram-staining test, so as to have included the steps of performing the above method on a wide array of bacteria (including gram-positive bacteria, and gram-negative bacteria, such as E. *aerogenes*), in order to have achieved the benefit of providing an effective means of identifying bacteria for use in treatment of conditions caused by septicemia.

Conclusion

14. No claims are allowable.

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014. Applicant is also invited to contact the TC 1600 Customer Service Hotline at (703) 308-0198.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alexander H. Spiegler
April 7, 2003

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
4/7/03